REMARKS

Claims 24 and 58-60 are pending and under examination in this application. In the Action, the Examiner rejected claims 24 and 58-60 under 35 U.S.C. §103(a) as assertedly obvious over Bostick et al., U.S. Patent No. 4,263,406 (hereinafter "Bostick"), in view of Grundy et al., U.S. Patent No. 6,991,810 (hereinafter "Grundy"). Applicants request reconsideration in light of the following amendment and remarks.

I. Support for Amendment to the Claims

Claim 24 is amended to insert "interfering substances in" to clarify the claimed invention. Support for this amendment is found, for example, at page 6, lines 5-17. This amendment includes no new matter.

II. Patentability

A. The rejection of claims 24 and 58-60 under 35 U.S.C. §103(a) as obvious over Bostick in view of Grundy should be withdrawn

The Examiner rejected claims 24 and 58-60 under 35 U.S.C. §103(a) as obvious over Bostick in view of Grundy. The Examiner asserts that Bostick discloses a device having an ion-exchange resin as an ion separator, and therefore, is capable of measuring and detecting glycosaminoglycans (GAGs). The Examiner further asserts that because Grundy teaches measurement of GAGs using the metachromatic dye DMMB, one of ordinary skill would readily combine the teachings of Bostick and Grundy to arrive at the present invention. Applicants respectfully disagree. As explained below, the Examiner has not provided an adequate rationale for why one of ordinary skill in the art would look to the detection reagents of Grundy as an obvious variation of the detection reagents of Bostick, since the species being detected in Bostick (isoenzymes) is different from the species being detected in Grundy (proteoglycans).

Claims 24 and 58-60 are directed to a GAG measuring device comprising a means for separating GAGs from a sample and a detection means, wherein the detection means is a detection reagent that binds the separated GAGs, and wherein the detection reagent is a metachromatic dye, such as DMMB. As explained below, neither Bostick nor

Grundy disclose a separator means for substantially separating GAGs from interfering substances, such as salt and protein, in a sample. Thus, even if improperly combined, Bostick and Grundy fail to disclose all elements of the claimed invention.

Bostick discloses an apparatus having an ion exchange column for separating a particular indicator species from a reaction solution, and discloses that components in the columns' effluent can be measured by comparative photometric means. Bostick teaches that a sample of interest is split into two sample streams, one of which is a reference stream and the other of which is useful to react the sample protein (enzyme) with a substrate in order to detect the reaction of the enzyme with the substrate, and detect turnover of the enzyme using an indicator species (see col. 5, lines 1-27). Bostick does not disclose the conditions under which the apparatus of Bostick can be enabled to separate and detect GAG moieties, which are not proteins, and certainly not enzymes as described in Bostick. Further, Bostick does not use as a detection means a reagent that binds to the separated GAG molecules, and, in particular, does not disclose detection of separated GAGs using a detection reagent, such as a metachromatic dye, that binds to the GAGs as recited in the claims.

Grundy describes isolation of *proteo*glycans, which are *proteins* having one or more polysaccharide moieties, from mucus of a starfish for use as an anti-fouling agent or an anti-inflammatory agent. Grundy describes that the level of proteoglycan in a sample may be measured using GAG content of the protein as a readout. The method described at col. 11, lines 28-40, cited by the Examiner, discloses that the *proteo*glycan is first cleaved by enzymes, the enzymatic digests are purified using ion exchange chromatography to determine if the *proteo*glycans are susceptible to cleavage by enzymes, and then the amount of *proteo*glycan in the digests is measured based on GAG content, using DMMB dye absorbance as a readout. Grundy neither discloses nor suggest separating GAGs from the protein portion of the *proteo*glycan as recited in the pending claims, nor describes adapting the method to conditions suited to isolate the GAG moieties.

To establish a *prima facie* case of obviousness, the Examiner must show that all the elements of the claim are taught or suggested in the prior art (MPEP 2143.03 and Federal Register Examination Guidelines for Determining Obviousness, Section III.A.1, Fed Reg., Vol 72, No. 195, 2007), and if all claim elements are described in the art, the

combination of elements must yield predictable results to render a claimed invention obvious. Further, it should be demonstrated that there was some teaching, suggestion or motivation in the prior art, or the knowledge generally available to an ordinary artisan, to combine the references, and that there was a reasonable expectation that such a combination would successfully result in the claimed invention (MPEP 2142 and Federal Register Examination Guidelines for Determining Obviousness, Section III.G, Fed Reg., Vol 72, No. 195, 2007). The Examiner must still provide "some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l. Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007) (quoting *In re Kahn,* 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir 2006)).

The Examiner has not established a *prima facie* case of obviousness because not all the elements of the claims are disclosed in the cited art, and further, the Examiner has not provided a rationale why one of ordinary skill would combine the teachings of Bostick and Grundy to arrive at the present invention. The specification describes that the device separates the GAGs by removing interfering materials, including cells, proteins, nucleic acids, neutral compounds and other small contaminating compounds, (page 16, lines 5-17). Neither Bostick nor Grundy describe conditions under which GAGs are separated from interfering molecules, including proteins, in a sample. On the contrary, Bostick describes isolation and detection of isoenzyme proteins and does not suggest that the enzymes comprise any GAG moieties. Grundy describes isolation of the entire *proteo*glycan molecule, not just the GAG portion of the proteoglycan, and does not disclose or suggest a method for isolating only the GAG portion of the proteoglycan. Further, the Examiner still has not provided evidence that the device disclosed in Bostick or the method in Grundy is adapted to separate and detect GAG moieties based on the conditions described in Bostick or Grundy, respectively, which only describe isolation of proteins. The Examiner also fails to explain how the skilled person reading Bostick or Grundy would recognize that the device of Bostick or the method of Grundy can be modified to separate and detect GAGs. Thus, not all the elements of the claimed invention are disclosed in the cited art.

Moreover, the Examiner misinterprets the teaching of Bostick with respect to detection reagent binding to the analyte. Bostick teaches detection of an indicator species,

but does not describe that the indicator species binds to the analyte, see e.g., col. 4, lines 58-69, or elsewhere in Bostick, as the Examiner suggests. For example, the detection means Bostick employs is direct photometric detection of the products of the enzymatic activity of separated isoenzymes, e.g, NADPH is used as a readout of creatine kinase activity in Example 1 (col. 7). While the substrate may bind to the isoenzymes, the enzymatic products being detected (e.g., NADPH) do not. Bostick thus fails to disclose "detection reagents that bind to separated glycosaminoglycan," as recited in the claims. Further, the detection means of Bostick could not possibly be adapted to detect GAG moieties because GAGs are not enzymes, and thus do not generate enzymatic products.

Additionally, the Examiner provides no objective reasoning why the skilled person would have been motivated to combine the disclosures of Bostick and Grundy to arrive at the claimed invention. The skilled person interested in improving detection of an indicator species using the device of Bostick would not have been motivated to use detection reagents that bind to the separated GAGs as in the present invention, since the indicator species itself, and not the actual isolated isoenzyme, is the detection reagent in Bostick. Nor would one of ordinary skill reading Bostick have looked to Grundy for guidance since Grundy teaches separation and detection of *proteo*glycans, not isoenzymes as taught in Bostick. Also, a person of ordinary skill interested in automating a procedure to separate and detect GAGs would not have looked to Grundy for guidance since Grundy teaches isolation of *proteo*glycans and not separated GAGs.

However, assuming *arguendo* that one of skill would have looked to Grundy for a method to detect GAGs in a sample, they would not have also looked to Bostick for guidance in isolation of GAGs because Bostick describes measurement of isoenzymes, not GAGs or even proteoglycans. As stated above, the Examiner must provide some rational underpinning to support a conclusion of obviousness, and the Examiner has not provided any evidence why one of ordinary skill reading Bostick would have been motivated to look to Grundy, and vice versa, when the two disclosures describe isolation of different types of proteins, and neither describes separation of GAG moieties.

As stated above, the disclosures of Bostick and Grundy, taken alone or in combination, fail to disclose each and every element of the claimed invention, and further,

the Examiner has provided no reason why one of ordinary skill in the art would have combined the teachings of Bostick and Grundy to arrive at the present invention. Therefore, the Examiner has failed to establish a *prima facie* case of obviousness and the rejection of claims 24 and 58-60 as obvious over Bostick in view of Grundy should be withdrawn.

III. Conclusion

Applicant submits that the application is in condition for allowance and respectfully request expedited notification of the same.

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Respectfully submitted,

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